Immuno-Ethiopia: Anti-leishmania Immunity

IUIS-FAIS Immuno-Ethiopia course co-sponsored by the IUIS, FAIS and Volkswagen Foundation took place between 23rd-29th of February. The theme of this meeting was Neglected Tropical Diseases and Malaria challenges in Sub-Saharan Africa. This week we highlight talks by Dr Fabienne Tacchini-Cottier (University of Lausanne, Switzerland) and Dr David Sacks (National Institutes of Health, USA) which focused on anti-leishmania immunity.

Dr Tacchini-Cottier gave an interesting lecture on the innate immunity to *Leishmania* parasites. She explained how the body recognizes the parasite by the PRRs and talked about the role of selected innate cells in immunity against the parasite. She also showed how the parasite has developed sophisticated ways to bypass the first barrier of immunity, the skin, and subvert the innate immune response permitting infection in different ways. Some of these immune evasion mechanisms include the role of *Leishmania* GP63 protein in degrading extracellular matrix and facilitating parasites' movement in the dermis and inactivation of the complement system by *Leishmania* parasite. She also explained the role of the inflammasome in Leishmania infection, emphasising that distinct Leishmania species can dampen NLRP3 activation as an evasion strategy.

Dr Tacchini-Cottier also highlighted the role of Neutrophils in leishmaniasis, which include active engulfment of *Leishmania* promastigotes and production of an array of

microbicidal factors against *Leishmania* such as nitric oxide, neutrophil elastase, platelet activating factor and neutrophil extracellular traps (NETs). In response to some of these mechanisms, some *Leishmania* species have developed various mechanisms to escape NET trapping and/or killing, as well as subvert macrophage killing and inhibit Denderitic cells function.

Dr Sacks lecture was on adaptive immunity against leishmaniasis, he explained that cutaneous Leishmaniasis infection of human hosts by *L. major* leads to the development of localized cutaneous lesions that eventually heal, and results in the generation of life-long immunity to re-infection. In the laboratory, most mouse genotypes control *L. major* infection, which is initiated typically by low dose needle inoculation of 100-1000 parasites into subcutaneous sites. This induces an IL-12-driven immunity which activates an IFN-γ-dominated Th1 response promoting healing and parasite clearance.

He has also explained the *"Infected Sand Fly Challenge Model"*, and how it has been used to determine the protective roles of memory CD4 T-cell subsets. Using this model, Dr Sacks suggests that only the effector CD4+ T cell subset and not central memory CD4 T cells confer protection against leishmaniasis infection.

Current rationale for leishmaniasis vaccine strategies aim to mimic natural protective immune response kinetics, however he suggests that this protective immune responses can be simply defined by the existence of memory cells. He suggested that the failure of Leishmania vaccines against CL may be related to the fact that conventional vaccines cannot maintain a population of pre-existing, terminally differentiated effector cells. He suggested that vaccines may have to accommodate the requirement for infection and/or persisting antigen to

establish and maintain the protective response.

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